Serial No. : 10/622,055 Filed : July 17, 2003

Applicant: Cernerud et al.

Page : 2 of 20

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously Presented) A compound of the general formula (I):

$$R^{5}$$
 R^{4}
 N
 N
 CH_{2}
 N
 CH_{2}
 M
 R^{3}
 N
 R^{1}
 R^{2}

(I)

wherein

m is 1 or 2;

n is 0, 1, 2, 3 or 4;

 R^1 is H, C_{1-6} -alkyl, aryl- C_1 - C_3 -alkyl, heteroaryl- C_1 - C_3 -alkyl, 2-hydroxyethyl, methoxy- C_2 - C_4 -alkyl, C_1 - C_4 -alkoxycarbonyl, aryloxy- C_2 - C_3 -alkyl, or heteroaryloxy- C_2 - C_3 -alkyl; wherein

any aryl or heteroaryl residue may be substituted with C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano; R^2 and R^3 each, independently, represent H or CH_3 ;

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1*H*-quinoxalin-2-one nucleus; and

R⁶ represents aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl; wherein

Serial No. : 10/622,055 Filed : July 17, 2003 Page : 3 of 20

any aryl or heteroaryl residue, alone or as part of another group, may be unsubstituted or substituted with one, two, three, four or five substituents, independently selected from aryl, aryl- C_{1-2} -alkyl, arylcarbonyl, heteroaryl, heteroaryl- C_{1-2} -alkyl, heteroarylcarbonyl, aryloxy, heteroaryloxy, arylthio, heteroarylthio, arylamino, heteroarylamino, C_{3-6} -cycloalkyl, C_{3-6} -cycloalkyloxy, C_{3-6} -cycloalkylcarbonyl, C_{1-6} -alkyl, C_{2-6} -alkanoyl, C_{2-6} -alkynyl, C_{2-6} -alkenyl, or fluoro- C_{2-4} -alkyloxy, halogen, trifluoromethyl, nitro, cyano, trifluoromethoxy, trifluoromethylthio, C_{1-6} -alkoxy, C_{1-6} -alkylthio, C_{1-6} -alkylamino, C_{1-4} -dialkylamino, hydroxy or oxo; wherein

any aryl or heteroaryl residue as substituents on aryl or heteroaryl, alone or as part of another group, in turn may be substituted in one or more positions, independently of each other, by C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

and pharmaceutically acceptable salts, hydrates, geometrical isomers, tautomers, optical isomers, or *N*-oxides thereof, with the provisos that:

R² and R³ are not both CH_{3;}

when n = 1 and R^1 , R^2 , R^4 and R^5 are H and R^3 is H or CH₃, then R^6 is not 3-pyridyloxy, 6-methyl-2-nitro-3-pyridyloxy, or 2-chloro-3-pyridyloxy;

when n = 0, then R^6 is not aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH or heteroaryl-NH; and

the compound of formula (I) is not 1-benzyl-3-(4-methyl-piperazin-1-yl)-1*H*-quinoxalin-2-one.

- 2. (Original) The compound according to claim 1, wherein any aryl or heteroaryl residue, alone or as part of another group, is substituted with one or two non-halogen substituents.
- 3. (Original) The compound according to claim 1, wherein

Reg

Serial No.: 10/622,055 Filed: July 17, 2003

Page : 4 of 20

any aryl or heteroaryl residue, alone or as part of another group, is substituted with at least one halogen substituent.

- 4. (Original) The compound according to claim 1 or 2, wherein any aryl or heteroaryl residue that is a substituent on another aryl or heteroaryl, alone or as part of another group, in turn is substituted in one position.
- 5. (Original) The compound according to claim 1, wherein

n = 1;

R¹, R², R³, R⁴ and R⁵ each are H; and

R⁶ is phenoxy, where the phenyl ring of the said phenoxy group may be unsubstituted or substituted with one, two, three, four or five substituents.

6. (Original) The compound according to claim 5, wherein the phenyl ring of R⁶ is substituted with one, two, three, four or five substituents independently selected from

halogen,

2-propenyl,

 C_1 - C_6 -alkyl,

 C_1 - C_6 -alkoxy,

trifluoromethyl,

phenyl,

phenoxy,

benzoyl, and

C₃-6-cycloalkyl;

wherein the phenyl, phenoxy or benzoyl substituent in turn may be unsubstituted or substituted in one or more positions, independently of each other, by C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano.

Reg

Serial No.: 10/622,055 Filed: July 17, 2003

Filed : July 17, 200 Page : 5 of 20

7. (Original) The compound according to claim 6, wherein the phenyl ring of R⁶ is substituted with one or two non-halogen substituents.

- 8. (Original) The compound according to claim 6, wherein the halogen substituent is fluorine.
- 9. (Original) The compound according to claim 1, wherein

$$n = 1$$
;

 R^1 is methoxy- C_2 - C_4 -alkyl or straight-chained C_1 - C_4 -alkyl;

R², R³, R⁴ and R⁵ each are H; and

R⁶ is 2,4,5-trifluorophenoxy.

10. (Original) The compound according to claim 1, wherein

$$n = 1$$
;

R¹, R², R³, R⁴ and R⁵ each are H; and

R⁶ is 2-oxo-1,3-benzoxathiol-5-yloxy.

11. (Original) The compound according to claim 1 wherein

$$n = 0$$
;

R¹, R², R³, R⁴ and R⁵ each are H; and

R⁶ is phenyl, where the said phenyl may be substituted with halogen, in one, two, three, four or five positions.

- 12. (Original) The compound according to claim 11 wherein the halogen is fluorine.
- 13. (Previously Presented) The compound according claim 1, which is:
 - 1-[2-(2-fluoro-4-nitrophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
 - $1-\{2-[(2-oxo-2H-chromen-7-yl)oxy]ethyl\}-3-(1-piperazinyl)-2(1H)-pyrazinone,$
 - 3-(1-piperazinyl)-1-[2-(2,4,5-trifluorophenoxy)ethyl]-2(1*H*)-pyrazinone,

Applicant : Cernerud et al.

Serial No. : 10/622,055

Attorney's Docket No.: 13425-122001 / BV-1031-US

Reg

Serial No.: 10/622,055 Filed: July 17, 2003 Page: 6 of 20

- 3-(1-piperazinyl)-1-[2-(2,3,5,6-tetrafluorophenoxy)ethyl]-2(1*H*)-pyrazinone,
- 1-[2-(2,3,4,5,6-pentafluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-chloro-2-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-cyclopentylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(1,2-benzisoxazol-3-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-methoxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-*n*-butyloxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-([1,1'-biphenyl]-3-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-(1-piperazinyl)-1-[2-(2,3,4-trifluorophenoxy)ethyl]-2(1*H*)-pyrazinone,
- 1-[2-(2,3-dichlorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(1,3-benzodioxol-5-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,4-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- $1-\{2-[(2-\infty-1,3-benzoxathiol-5-yl)oxy]ethyl\}-3-(1-piperazinyl)-2(1H)-pyrazinone,$
- 1-[2-(3-hydroxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-(1-piperazinyl)-1-[2-(6-quinoxalinyloxy)ethyl]-2(1*H*)-pyrazinone,
- $1-\{2-[3-(N,N-\text{dimethylamino})\text{phenoxy}]\text{ethyl}\}-3-(1-\text{piperazinyl})-\text{pyrazin-}2(1H)-\text{one},$
- 3-(1-piperazinyl)-1-{2-[3-(trifluoromethyl)phenoxy]ethyl}-2(1H)-pyrazinone,
- 1-[2-(3-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-nitrophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-benzoylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3,5-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(phenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,6-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2-cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(4-trifluoromethylphenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(4-bromophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-{4-phenoxy-(phenoxy)}ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,

Serial No.: 10/622,055 Filed: July 17, 2003 Page: 7 of 20

• 1-[2-(4-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,

- 1-[2-(4-isopropylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,4,5-trichlorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2-methylthiophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-methoxyphenylthio)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-{(4-allyl-2-methoxy)phenoxy}ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(5,6,7,8-tetrahydro-naphthalen-2-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,6-difluorophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-trifluoromethylphenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-bromophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(phenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1*H*)-pyrazinone,
- 1-[2-(4-fluorophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-[2-(4-isopropylphenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-[2-(2-methylthiophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1*H*)-pyrazinone,
- 1-(2,4,5-trifluorobenzyl)-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[3-(2,4,5-trifluorophenyl)propyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-(2,3-dihydro-benzo[1,4]dioxin-2-ylmethyl)-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-piperazin-1-yl-1[2-(2,4,5-trifluoro-phenoxy)-ethyl]-1*H*-quinoxalin-2-one,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-n-butyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-[4-(2-methoxyethyl)-1-piperazinyl]-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-isopropyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-{2-[(5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-7-yl)oxy]ethyl}-3-(1-piperazinyl)-2(1*H*)-pyrazinone,

Applicant : Cernerud et al.

Attorney's Docket No.: 13425-122001 / BV-1031-US

Serial No. : 10/622,055

Serial No. : 10/622,055 Filed : July 17, 2003 Page : 8 of 20

- 1-[2-(4-Cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[4-(2,4,5-trifluorophenoxy)butyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[3-(2,4,5-trifluorophenoxy)propyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-[4-(1-phenylethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1*H*)-one,
- 3-[4-(2-phenoxyethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1*H*)-one,
- 3-[4-(2-Phenylethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1*H*)-one, hydrochloride,
- 3-(4-Benzylpiperazin-1-yl)-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1*H*)-one hydrochloride,
- 3-[(2R)-2-methylpiperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1H)-one,
- 3-piperazin-1-yl-1-[2-(3-thienyl)ethyl]pyrazin-2(1*H*)-one,
- 3-piperazin-1-yl-1-[2-(2-thienyl)ethyl]pyrazin-2(1*H*)-one,
- 1-[2-(1H-indol-3-yl)ethyl]-3-piperazin-1-ylpyrazin-2(1*H*)-one,
- 1-[2-(2,3-dihydro-1,4-benzodioxin-5-yloxy)ethyl]-3-piperazin-1-ylpyrazin-2(1*H*)-one,
- 1-[2-(phenylthio)ethyl]-3-piperazin-1-ylpyrazin-2(1H)-one,
- 1-(3-oxo-3-phenylpropyl)-3-piperazin-1-ylpyrazin-2(1*H*)-one, or
- 1-[3-(4-fluorophenyl)-3-oxopropyl]-3-piperazin-1-ylpyrazin-2(1*H*)-one, and their pharmacologically acceptable salts and hydrates.
- 14. (Original) A pharmaceutical composition comprising a compound according to claim 1 as an active ingredient, together with a pharmaceutically acceptable carrier.
- 15. (Cancelled)
- 16. (Previously Presented) A method for the treatment of a disorder or medical condition selected from angina; Raynaud's phenomenon; intermittent claudication; coronary or

Applicant : Cernerud et al. Serial No. : 10/622,055 Filed : July 17, 2003

Filed : July 17, 2003 Page : 9 of 20

peripheral vasospasms; hypertension; schizophrenia; obsessive-compulsive disorder; attention deficit hyperactivity disorder (ADHD); anxiety disorders; depression disorders substance abuse; extrapyramidal symptoms; menopausal and post-menopausal hot flushes; premenstrual syndrome; bronchoconstriction disorders; or eating disorders, the method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.

17. (Cancelled)

- 18. (Currently Amended) A method for the treatment of a disorder or medical condition that is associated with neuroleptic drug-induced extrapyramidal symptoms therapy, the method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.
- 19. (Previously Presented) The method according to claim 16 wherein the eating disorder is binge eating disorders, anorexia nervosa or bulimia.
- 20. (Cancelled)
- (Currently Amended) A method of making a compound of formula (I) according to claim

 wherein R⁶ is selected from aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, or heteroaryl-NH,

by reacting a compound of the following formula (II):

$$R^{5}$$
 N
 O
 $(CH_{2})m$
 R^{3}
 N
 R^{1}
 R^{2}
 (II)

Reg

Serial No.: 10/622,055 Filed: July 17, 2003

 R^{5} N O $(CH_{2})n$ X R^{4} N $(CH_{2})m$ R^{1} R^{2} (III)

wherein

Applicant: Cernerud et al.

: 10 of 20

Page

m is 1 or 2;

n is 1 or 2;

X is OH;

 R^1 is H, C_{1-6} -alkyl, aryl- C_1 - C_3 -alkyl, heteroaryl- C_1 - C_3 -alkyl, 2-hydroxyethyl, methoxy- C_2 - C_4 -alkyl, C_1 - C_4 -alkoxycarbonyl, aryloxy- C_2 - C_3 -alkyl, or heteroaryloxy- C_2 - C_3 -alkyl; wherein

any aryl or heteroaryl residue may be substituted with C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano; R^2 and R^3 each, independently, represent H or CH_3 ; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1*H*-quinoxalin-2-one nucleus;

with an optionally substituted phenol or thiophenol; in a solvent.

- 22. (Original) A method according to claim 21 for the preparation of compounds of formula (I) where R¹ is H, wherein R¹ in the corresponding intermediate of formula (II) is a protecting group selected from *tert*-butoxycarbonyl (*t*-BOC) or trityl.
- 23. (Original) A method according to any one of claims 21 or 22, wherein the intermediate of formula (II) is selected from:

2-[3-(4-*tert*-butoxycarbonyl-3-methyl-1-piperazinyl)-pyrazinyloxy]ethanol; *tert*-Butyl (3*R*)-4-[3-(2-hydroxyethoxy)pyrazin-2-yl]-3-methylpiperazine-1-carboxylate;

Reg

Serial No.: 10/622,055 : July 17, 2003 Filed

Applicant: Cernerud et al.

Page : 11 of 20

and

tert-Butyl 4-[3-(2-hydroxyethoxy)pyrazin-2-yl]-1,4-diazepane-1-carboxylate.

24. (Currently Amended) A method of preparing a compound of formula (I) according to claim 1,

wherein R⁶ is selected from aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl, by reacting a compound of the following formula (IV),

wherein

m is 1 or 2;

Hal is halogen;

 R^1 is H, C_{1-6} -alkyl, aryl- C_1 - C_3 -alkyl, heteroaryl- C_1 - C_3 -alkyl, 2-hydroxyethyl, methoxy-C₂-C₄-alkyl, C₁-C₄-alkoxycarbonyl, aryloxy-C₂-C₃-alkyl, or heteroaryloxy-C₂-C₃-alkyl; wherein

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano; R² and R³ each, independently, represent H or CH₃; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1H-quinoxalin-2-one nucleus; with an alkali metal or alkaline earth metal basic salt, in aqueous media, at 25 to 150 °C, to produce a compound of formula (V),

Serial No.: 10/622,055 : July 17, 2003 Filed

Applicant: Cernerud et al.

Page : 12 of 20

$$R^{5}$$
 N
 N
 C
 CH_{2}
 M
 R^{3}
 N
 R^{1}
 R^{2}
 (V)

wherein

m is 1 or 2;

 R^1 is H or C_{1-6} -alkyl, aryl- C_1 - C_3 -alkyl, heteroaryl- C_1 - C_3 -alkyl, 2-hydroxyethyl, methoxy-C₂-C₄-alkyl, C₁-C₄-alkoxycarbonyl, aryloxy-C₂-C₃-alkyl, or heteroaryloxy-C₂-C₃-alkyl; wherein

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano; R² and R³ each, independently, represent H or CH₃; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1*H*-quinoxalin-2-one nucleus; followed by N-alkylation of the compound of formula (V) by reaction with a compound of formula (VI),

$$R^6-CH_2-(CH_2)_n-Y$$
 (VI)

wherein

n is 0, 1, 2, 3 or 4;

Y is a leaving group; and

R⁶ represents aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl; and

wherein any aryl or heteroaryl residue, alone or as part of another group, may be unsubstituted or substituted. Where substituted, one, two, three, four or five substituents may be present, preferably one or two for non-halogen substituents, and are independently selected from aryl, aryl-C₁₋₂-alkyl, arylcarbonyl, heteroaryl, heteroaryl-C₁₋₂-alkyl, heteroarylcarbonyl, aryloxy,

Reg

Applicant: Cernerud et al. Serial No.: 10/622,055 Filed: July 17, 2003 Page: 13 of 20

heteroaryloxy, arylthio, heteroarylthio, arylamino, heteroarylamino, C_{3-6} -cycloalkyl, C_{3-6} -cycloalkyloxy, C_{3-6} -cycloalkylcarbonyl, C_{1-6} -alkyl, C_{2-6} -alkanoyl, C_{2-6} -alkenyl, or fluoro- C_{2-4} -alkyloxy, halogen, trifluoromethyl, nitro, cyano, trifluoromethoxy, trifluoromethylthio, C_{1-6} -alkoxy, C_{1-6} -alkylthio, C_{1-6} -alkylamino, C_{1-4} -dialkylamino, hydroxy or oxo;

wherein any aryl or heteroaryl residue as substituents on aryl or heteroaryl, alone or as part of another group, in turn may be substituted in one or more positions, preferably one, independently of each other by C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy, or cyano;

in the presence of a base in a suitable solvent at an elevated temperature.

- 25. (Original) A method according to claim 24 for the preparation of compounds of formula (I) where R¹ is H, wherein R¹ in the corresponding intermediate of formula (V) is a protecting group selected from tert-butoxycarbonyl (t-BOC) or trityl.
- 26. (Original) The method according to claim 22 wherein R¹ in the corresponding intermediate of formula (II) is tert-butoxycarbonyl (t-BOC).
- 27. (Original) The method according to claim 25 wherein R¹ in the corresponding intermediate of formula (V) is tert-butoxycarbonyl (t-BOC).
- 28. (Original) The compound according to claim 1 where in the compound of formula (I)

$$n = 1$$
;
 R^1 is aryl-C1-C3-alkyl;
 R^2 , R^3 , R^4 and R^5 are each H; and
 R^6 is 2,4,5-trifluorophenoxy.

Reg

Serial No.: 10/622,055

Filed : July 17, 2003 Page : 14 of 20

29. (Previously Presented) A method for the treatment of glaucoma, the method comprising administering to a subject in need thereof a therapeutically effective amount of a

compound according to claim 1.

30. (Previously Presented) The method of claim 29, wherein the glaucoma is normal tension

glaucoma.

31. (Previously Presented) A method for the treatment of urinary incontinence, the method

comprising administering to a subject in need thereof a therapeutically effective amount

of a compound according to claim 1.

32. (Previously Presented) The method of claim 31, wherein the urinary incontinence is

urinary incontinence with co-existing diabetes.

33. (Previously Presented) The method of claim 16, wherein the depression disorder is

depression with coexisting diabetes.

34. (Cancelled)

35. (Cancelled)

36. (Currently Amended) A method for the treatment of sleep disorders insomnia or sleep

apnea, the method comprising administering to a subject in need thereof a therapeutically

effective amount of a compound according to claim 1.

37. (Cancelled)

38. (Cancelled)

39. (Cancelled)

Serial No.: 10/622,055 Filed: July 17, 2003

Page : 15 of 20

40. (Currently Amended) A method for the treatment of thrombotic illness thrombosis, the method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.

- 41. (Cancelled)
- 42. (Cancelled)
- 43. (Cancelled)
- 44. (Currently Amended) A method for the treatment of diabetic complications <u>selected from</u> <u>nephropathy</u>, neuropathy and retinopathy, the method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to claim 1.